# Rh isoimmunization during pregnancy: antenatal prophylaxis

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**Of 3533 Rh-negative women who began a pregnancy without detectable Rh antibodies, 62 (1.8%) demonstrated evidence of Rh isoimmunization during pregnancy or within 3 days after delivery. All denied transfusions as well as abortions or previous pregnancies not followed by the administration of Rh immune globulin. Rh isoimmunization during pregnancy or within 3 days after delivery, which will not be prevented by the administration of Rh immune globulin after delivery, is the most important cause of residual Rh isoimmunization. A clinical trial of antenatal administration of Rh immune globulin, initially at 34 weeks' and subsequently at 28 and 34 weeks' gestation, in 1357 Rh-negative pregnant women who were delivered of Rh-positive babies, was effective in preventing the development of Rh isoimmunization during pregnancy or within 3 days after delivery. Antenatal prophylaxis with Rh immune globulin will be necessary if the incidence of Rh isoimmunization is to be reduced to its lowest possible level. Antenatal prophylaxis at 28 weeks' gestation is now an insured service in Manitoba.**

**Sur 3533 femmes Rh négatif qui ont entrepris une grossesse sans anticorps anti-Rh décelables, 62 (1.8%) ont démontré des signes d'isoimmunisation Rh durant la grossesse ou durant les 3 jours qui ont suivi l'accouchement. Toutes ont nié une transfusion ainsi qu'un avortement ou une grossesse antérieure qui n'aurait pas été suivi de l'administration d'immunoglobuline Rh. L'isoimmunisation durant la grossesse ou les 3 jours consécutifs à l'accouchement, qui ne peut être prévenue par l'administration d'immunoglobuline Rh après l'accouchement, est la plus importante cause d'isoimmunisation Rh résiduelle. Un essai clinique de l'administration prénatale d'immunoglobuline Rh, initialement à la 34e semaine et, par la suite, à la 28e et à la 34e semaine de gestation, chez 1357 femmes enceintes Rh négatif qui ont donné naissance à des bébés Rh positif, a permis de prévenir efficacement le développement d'une isoimmunisation durant la grossesse ou les 3 jours consécutifs à l'accouchement. La prophylaxie prénatale avec l'immunoglobuline Rh sera nécessaire si l'on veut réduire la fréquence de l'isoimmunisation Rh au niveau le plus bas possible. La prophylaxie prénatale à la 28e semaine de gestation est maintenant un service couvert par les régimes d'assurance au Manitoba.**

Before 1967 approximately 7% to 8% of Rh-negative women delivering Rh-positive, ABO-compatible babies[1,2] and 1% of those delivering Rh-positive, ABO-incompatible babies[3] became Rh isoimmunized within 6 months after delivery. About the same proportions of women had no evidence of Rh isoimmunization 6 months after delivery but, by producing a secondary Rh immune response in their next Rh-positive pregnancy, indicated that they had been isoimmunized as a result of the first pregnancy, the concentrations of Rh antibody, however, being too low to be detected by the screening methods used.[4]

The Western Canada Rh prevention trial[1] showed, as did all such trials, that intramuscular administration of a Cohn-fractionated immune globulin manufactured from plasma with a very high Rh antibody content ($Rh_0$ [D] immune globulin; Connaught Laboratories, Toronto) was effective in preventing Rh isoimmunization when it was given in doses of 145 to 435 $\mu$g within 3 days after delivery. No "failures of prevention" were found among women with no evidence of Rh isoimmunization at the time of the injection. It was on the basis of this trial that Rh immune globulin was licensed for clinical use in Canada in December 1968. One standard prophylactic dose (about 300 $\mu$g) was to be given within 72 hours after delivery to all Rh-negative women without evidence of Rh isoimmunization who had aborted or been delivered of Rh-positive infants.

## Rh antibody screening and titration

All pregnant Rh-negative women in Manitoba have Rh antibody screening tests carried out by the Rh laboratory during pregnancy and after delivery. Their serum is screened by a manual two-stage technique that uses erythrocytes treated with Löwe's papain (M. Lewis and B. Chown: unpublished method). In 1971 bromelin[5] and low-ionic[6] AutoAnalyzer screening methods were added; the bromelin method was discontinued in 1974. If an antibody is detected its specificity and its titre are determined by saline,[7] albumin[8] and indirect antiglobulin[9] methods.

The enzyme and AutoAnalyzer screening methods used by the Rh laboratory are very sensitive and will detect the presence of Rh antibodies that would not be demonstrated by indirect antiglobulin methods, which are not infrequently the only screening methods used by hospital blood bank laboratories.

## Remaining problems in Rh prevention

There are five major residual problems in Rh prophylaxis:

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1. Failure to treat with Rh immune globulin because the Rh status of the mother is unknown or because there has been a breakdown in prenatal or intrapartum care.

2. Failure to recognize the hazards of transplacental hemorrhage at the time of amniocentesis for genetic study in early pregnancy or for determination of gestational age in later pregnancy, and failure to administer Rh immune globulin at the time of amniocentesis if the woman is Rh-negative.

3. Failure to remember that the Rh-negative woman who has a therapeutic or a spontaneous abortion has a 2% to 3% risk of Rh isoimmunization if she is not given Rh immune globulin at the time of abortion.

4. Failure of one dose (300 $\mu$g) of Rh immune globulin to protect because of massive transplacental hemorrhage; 0.1% of Rh-negative mothers will become Rh isoimmunized because of undiagnosed transplacental hemorrhage in excess of 30 mL of fetal blood.

5. The Rh-negative woman who becomes Rh isoimmunized during pregnancy or within 3 days after delivery, prior to administration of Rh immune globulin.

The first three problems can be solved by further education of the pregnant woman and of those delivering health care to her. The fourth can be solved only by routine use of the Kleihauer fetal-cell screening test (which does not lend itself to routine laboratory use) and by administration of at least 10 $\mu$g of anti-D per millilitre of maternal blood that has passed into the fetus. However, failures of Rh prevention due to the fourth problem are very few. The most important residual problem in Rh prophylaxis in Manitoba is the fifth.

## Rh isoimmunization during pregnancy

During the period Mar. 1, 1967 to Dec. 15, 1974, 62 of 3533 Rh-negative women in Manitoba showed evidence of Rh isoimmunization during pregnancy or within 3 days after delivery (Table I). All were either primigravidas with no history of blood transfusion or abortion, or multigravidas with no prior evidence of Rh isoimmunization who had been given Rh immune globulin after all previous Rh-positive abortions and deliveries. The overall incidence of Rh isoimmunization in this series was 1.8% (2.0% when the baby was ABO-compatible, 0.6% when ABO-incompatible).

Of the 62 instances of Rh isoimmunization, in 42 the antibody could first be detected (Table II) only by enzyme and AutoAnalyzer techniques* and not by indirect antiglobulin methods. By 3 days after delivery the Rh antibody in 29 of the 42 was still not detectable by indirect antiglobulin methods but in 13 of the 29 was demonstrable by a sensitive capillary saline method, indicating the presence of an IgM antibody. Thus, if enzyme and AutoAnalyzer screening methods had not been available and indirect antiglobulin and saline techniques alone had been used, 46 (74%) of the women would have been identified as Rh isoimmunized at the time of delivery; the remaining 16 (26%) would not. These figures are of importance when one comes to consider the results of antenatal Rh prophylaxis. Since passive Rh antibody given 12 and 6 weeks before delivery will mask active isoimmunization demonstrable only by enzyme and AutoAnalyzer methods (26% of instances), one would expect to be able to detect 74% of failures of antenatal Rh prophylaxis at the time of delivery.

Of the 62 women found to be Rh isoimmunized during pregnancy or within 3 days after delivery 50 (81%) still had Rh antibodies detectable 6 to 9 months after delivery, at a time when passive antibody would have disappeared. Therefore, 6 to 9 months after delivery Rh antibody screening would demonstrate the failure of Rh prophylaxis in 81% of instances; in the remaining 19% it would become manifest only during a subsequent Rh-positive pregnancy.

In 5 of the 62 women (8%) (Table III) the Rh antibodies were detectable prior to 29 weeks' gestation (3 primigravidas at 11, 25 and 28 weeks' and 12 multigravidas at 23 and 27 weeks' gestation). These five patients would not have been protected by Rh immune globulin given at 28 weeks' gestation. The woman who had an Rh antibody at 11 weeks' gestation had no previous

**Table I—Rh isoimmunization during pregnancy or within 3 days after delivery, Manitoba, Mar. 1, 1967 to Dec. 15, 1974**

| Blood group of baby | No. of Rh-negative pregnant women | | No. (and %) Rh isoimmunized | | | |
|---|---|---|---|---|---|---|
| **Rh-positive, ABO-compatible** | | | | | | |
| All women | 2859 | | 58 | (2.0) | | |
| Primigravidas | | 2257 | | 44 | | (1.9) |
| Multigravidas | | 602 | | 14 | | (2.3) |
| **Rh-positive, ABO-incompatible** | | | | | | |
| All women | 674 | | 4 | (0.6) | | |
| Primigravidas | | 511 | | 1 | | (0.2) |
| Multigravidas | | 163 | | 3 | | (1.8) |
| **Total** | | | | | | |
| All women | 3533 | | 62 | (1.8) | | |
| Primigravidas | | 2768 | | 45 | | (1.6) |
| Multigravidas | | 765 | | 17 | | (2.2) |

**Table II—Characteristic of Rh antibody in 62 of the Rh-negative isoimmunized women**

| Time | Characteristic of Rh antibody | | |
|---|---|---|---|
| | Strong* | Weak† | No longer demonstrable |
| When first detected | 20 | 42 | – |
| Within 3 days after delivery | 33‡ | 29§ | – |
| Six to 9 months after delivery | 39 | 11 | 12 |
| When last tested | 43 | 11 | 8 |

*Demonstrable not only by enzyme and AutoAnalyzer methods but also by indirect antiglobulin and usually albumin techniques.
†Demonstrable by manual enzyme and AutoAnalyzer methods but not by indirect antiglobulin techniques.
‡Of the 33 women 27 were delivered of direct-Coombs'-positive affected babies and a further 9 (total 36) were delivered of direct-Coombs'-positive affected babies in a subsequent pregnancy.
§In 13 of the 29, although the Rh antibody could not be detected by albumin or indirect antiglobulin techniques, it could be detected by saline methods indicating the presence of IgM anti-D and hence active Rh isoimmunization, which would not be masked by passive Rh antibody if Rh immune globulin had been given.

*The instance of a woman having in her serum an Rh antibody detectable only by an AutoAnalyzer method is recorded as such but is not considered to be one of proven isoimmunization until the antibody can also be detected at least by the two-stage manual enzyme method. Some Rh antibodies detectable only by AutoAnalyzer react best at room temperature and never increase in strength. Such instances may not be examples of specific Rh isoimmunization.

Table III—Time of first positive antibody test in the 62 women

| Time | Primigravidas | Multigravidas | All women |
|---|---|---|---|
| Gestation (weeks) | | | |
| 0–13 | 1 | 0 | 1* |
| 14–20 | 0 | 0 | 0 |
| 21–28 | 2 | 2 | 4† |
| 29–34 | 3 | 7 | 10‡ |
| 35–40 | 15 | 5 | 20 |
| Immediately after delivery | 14 | 3 | 17 |
| Three days after delivery | 10 | 0 | 10 |
| Total | 45 | 17 | 62 |

*Rh antibody noted in first test at 11 weeks' gestation. The woman's mother was Rh-positive; Rh isoimmunization may have been due to maternal-fetal transplacental transfusion.
†Rh antibody noted at 23 to 28 weeks' gestation — too early for antepartum Rh prophylaxis at 28 weeks' gestation to be effective.
‡Rh antibody noted at 29 to 34 weeks' gestation — too early for antepartum Rh prophylaxis at 34 weeks' gestation to be effective.

negative tests and her mother was Rh-positive; it is conceivable that this was an instance of Rh isoimmunization due to maternal–fetal transplacental hemorrhage. The other four instances, as far as we can determine, were ones of Rh isoimmunization during pregnancy, although we are not so naive as to believe that we are being told the truth regarding past pregnancies and abortions in every instance.

Ten women in this group (16%) first demonstrated evidence of Rh isoimmunization between 29 and 34 weeks' gestation and would not have been protected by Rh immune globulin given as early as 34 weeks' gestation. The remaining 47 (76%) demonstrated Rh antibodies initially between 35 weeks' gestation and 3 days after delivery.

In considering the evidence that Rh isoimmunization occurred in a particular pregnancy it must be kept in mind that in some cases the frequency of antibody screening during pregnancy was far from ideal. Although blood samples were requested every 4 weeks, in 20 of the 62 women the interval between the last negative test and the first positive test was 8 to 30 weeks. In another four (all primigravidas) there were no preceding negative tests. In one of the four the isoimmunization was discovered at 11 weeks' gestation, in another the antibody was demonstrated at 25 weeks and in the remaining two it was demonstrated at delivery. All four denied previous pregnancies, abortions and transfusions. In the remaining 38 there was a preceding negative test within 4 weeks in 26, within 2 weeks in 8 and within 3 days in 4. Therefore, the time at which Rh isoimmunization occurred may have been considerably earlier than that recorded for 24 of the 62 women.

That the development of Rh isoimmunization during pregnancy or within 3 days after delivery may have serious consequences is shown by the data in Table IV; 17 of the 62 women have completed another Rh-positive pregnancy. The blood of 12 of the 17 babies was direct-Coombs'-positive. Two (12%) required intrauterine fetal transfusions to survive and another three (18%) required early delivery and exchange transfusions. Two (12%) would have required exchange transfusions in the prephototherapy era. Thus, 7 of 17 (41%) required prompt and vigorous treatment.

### Antenatal Rh prophylaxis trial

In December 1968 a trial of antenatal Rh prophylaxis in Winnipeg was begun. Initially, Rh-negative primigravidas who were to be delivered in two Winnipeg hospitals were given one injection of Rh immune globulin (approximately 300 $\mu$g) at 34 weeks' gestation; women who were to be delivered at the other three hospitals in the city were not treated antenatally. In May 1969, because of evidence that some women were becoming Rh-isoimmunized before 34 weeks' gestation, an injection was given at 28 weeks in addition to the one at 34 weeks. In January 1972, because sufficient untreated women had been accumulated to serve as controls, antenatal prophylaxis was offered to all Rh-negative women whose delivery was to take place in Winnipeg hospitals. All women in the trial (those treated and those not treated antenatally) were given Rh immune globulin postnatally if they were delivered of Rh-positive babies; those who were delivered of Rh-negative babies were excluded from the trial. Women who entered as primigravidas re-entered the trial in all subsequent pregnancies.

Table IV—Outcome of 17 subsequent Rh-positive pregnancies in the 62 women

| Outcome | No. of pregnancies |
|---|---|
| Fetal and exchange transfusion required | 2 |
| Exchange transfusion and early delivery required | 3 |
| Phototherapy required | 2 |
| Direct-Coombs'-positive; treatment not required | 5 |
| Direct-Coombs'-negative; unaffected | 5 |

Maternal blood samples were tested at 28 weeks' gestation and every 2 weeks until delivery, immediately after delivery, 3 days after delivery prior to the injection of Rh immune globulin, then 6 weeks, 4 months and 6 months after delivery. Women with passive antibody still demonstrable 6 months after delivery were retested at 9 months. The sera were screened for Rh antibody by saline and two-stage papainized erythrocyte manual methods and by AutoAnalyzer techniques (both bromelin and low ionic from 1971 to 1974, low ionic only since 1974). Blood samples obtained during pregnancy and those obtained immediately after and 3 days after delivery were screened for fetal transplacental hemorrhage by the Kleihauer method.[10] Cord blood samples were tested for ABO and Rh antigens and by the direct Coombs' test. Cord hemoglobin and serum bilirubin values were also determined.

Before we embarked on the antenatal Rh prophylaxis trial we believed that the small amount of Rh antibody that traversed the placenta would not harm the Rh-positive fetus. In 25 years of experience with Rh isoimmunization we have found that Rh isoimmunized women with Rh antibody titres equivalent to or higher than those achieved by the injection of 300 $\mu$g of Rh immune globulin at 6-week intervals (albumin titre 1:1 or 1:2) invariably produce babies who, although direct-antiglobulin-positive, have no clinical evidence of erythroblastosis.

This belief was upheld by our observations in the antepartum prophylaxis trial. Although 28% of ABO-compatible and 47% of ABO-incompatible Rh-positive cord blood samples were weakly direct-antiglobulin-positive, no baby showed evidence of anemia. Cord serum bilirubin values never exceeded 3.4 mg/dL. Hyperbilirubinemia severe enough to require phototherapy did not develop in the ABO-compatible babies, although occasionally it did in ABO-incompatible babies, probably because of ABO erythroblastosis.

*Results*

A total of 1357 women given Rh immune globulin, 1204 at 28 and 34 weeks' gestation and 153 at 28 or 34 weeks' gestation, subsequently were delivered of Rh-positive babies (Table V). One would have expected 24 (1.8%) of the 1357 to be isoimmunized during pregnancy or within 3 days after delivery if antenatal prophylaxis were un-

Table V—Results of Winnipeg antenatal Rh prophylaxis trial, Dec. 1, 1968 to Aug. 31, 1976

| Datum | No. of deliveries | No. followed up for 6 to 9 months |
|---|---|---|
| Prophylaxis: 300 μg of Rh immune globulin given at 28 and 34 weeks' gestation | | |
| Rh-positive babies | 1204 | 905 |
| ABO-compatible babies | 925 | 683 |
| 28 or 34 weeks' gestation | | |
| Rh-positive babies | 153 | 99 |
| ABO-compatible babies | 117 | 76 |
| Total Rh-positive | 1357 | 1004 |
| Total ABO-compatible | 1042 | 759 |
| Rh isoimmunization | | |
| Expected (1.8%) | 24 | 18 |
| Not obscured by passive antibody | 18 | — |
| Persisting at 6 to 9 months | — | 15 |
| Observed | 0 | 0* |

*One woman with what appeared to be persisting passive Rh antibody 6 months after delivery was lost to follow-up at 9 months. She in no way differed from 12 others with similar weak passive Rh antibodies at 6 months who had no demonstrable Rh antibodies 9 months after delivery.

successful. In 18 (75%) of the 24 failure would not have been obscured by passive Rh antibody. No examples of Rh isoimmunization were found at delivery.

If antenatal prophylaxis had been unsuccessful one would have expected to find 81% of 1.8% of 1004 (15) women to have evidence of Rh isoimmunization 6 to 9 months after delivery. None showed such evidence.

Of 413 Rh-negative women treated antenatally and delivered of Rh-positive babies who had subsequent pregnancies, 343 had babies who also were Rh-positive. If antenatal prophylaxis had been unsuccessful but evidence of isoimmunization had been obscured at delivery and was no longer demonstrable 6 to 9 months after delivery, we would have expected 6 (1.8%) of the 343 to have demonstrated a secondary immune response by the end of the 2nd or during the 3rd trimester; none of the 343 showed evidence of such a response.

## Discussion

Although it may be surprising that 62 of 3533 Rh-negative women who at the commencement of an Rh-positive pregnancy were without evidence of Rh isoimmunization showed indications of such immunization during pregnancy or within 3 days after delivery, the evidence is conclusive.

Alternative explanations for this phenomenon, other than primary Rh isoimmunization during pregnancy, must be considered. It is possible that women apparently immunized during pregnancy or within 3 days after delivery may have been immunized by a prior unrecognized or concealed pregnancy. We can only state that these women were interviewed in confidence either by ourselves or by the family obstetrician. It is unlikely that all 62 (or even a substantial proportion) were not telling the truth. If a prior pregnancy were the cause of the observed Rh isoimmunization, one would not expect antenatal Rh prophylaxis to be successful unless repeated injections of Rh immune globulin can suppress or reverse very early weak Rh isoimmunization.

Another possibility is that these women were Rh isoimmunized in utero by maternal–fetal transplacental transfer of erythrocytes if their mothers were Rh-positive, such isoimmunization being very weak or no longer demonstrable years later when they embarked upon their first pregnancies. Indeed, one could invoke this cause in the woman noted to be isoimmunized at the first test in her first pregnancy at 11 weeks' gestation. Although we have not made a determined effort to obtain blood samples from the mothers of our 62 Rh-negative women, we have had occasion to obtain blood from 8 of them; 37.5% (3) were Rh-positive, a proportion not significantly different from the approximately 60% overall proportion of Rh-positive mothers of Rh-negative offspring. We are now studying this problem but have no evidence that transplacental passage of blood from mother to fetus with subsequent Rh isoimmunization in infancy is a significant cause of the isoimmunization that we observed in these women. Again, if this were an important cause of early isoimmunization, one would not expect antenatal prophylaxis to be successful unless, as already speculated, Rh prophylaxis has a suppressive effect on early Rh isoimmunization.

Antibody screening studies have always been carried out in Winnipeg with the use of sensitive techniques. If indirect antiglobulin screening methods alone had been used, many of the examples of Rh isoimmunization during pregnancy in our series would have been missed initially or altogether, to appear in subsequent pregnancies as failures of Rh prophylaxis. It is probable that the apparent high incidence of Rh isoimmunization during pregnancy in Manitoba is related to the sensitivity of the antibody screening techniques used and that Rh immune globulin (i.e., passive prophylaxis) will always prevent Rh isoimmunization, provided it is given early enough (i.e., prior to active immunization) and in sufficient dose.

Since at least 0.14% of instances of Rh isoimmunization (8% of 1.8%) will be noted before 29 weeks' gestation, one cannot expect that a program in which antenatal Rh prophylaxis is given initially at 28 weeks' gestation will ensure complete protection. It would be reasonable to expect the failure rate to decrease from 1.8% to 0.14%. During our trial, one of the five women whose Rh isoimmunization was noted before 29 weeks' gestation would otherwise have been a candidate (a failure rate of 0.07%).

Whether the 1.8% incidence of Rh isoimmunization noted during pregnancy or within 3 days after delivery is completely or almost completely due to primary isoimmunization during pregnancy or due to a secondary immune response in women very weakly Rh isoimmunized by unknown or undisclosed abortions or pregnancies, or by maternal–fetal transfusion, the evidence for the protection conferred by an antenatal prophylaxis program is irrefutable. The incidence of Rh isoimmunization during pregnancy or within 3 days after delivery has been reduced from 1.8% to 0.07%. The likelihood of such a difference occurring by chance is less than 1 in 10 000.

Antenatal Rh prophylaxis has been accepted by the Manitoba Health Services Commission as an insured service and is provided to all Rh-negative unimmunized pregnant women at risk in the province. Because a single vial of 300 μg of Rh immune globulin produces passive antibody concentrations that are still detectable at 3 months and because, on theoretical grounds, one would expect that there would still be about 30 μg of residual Rh immune globulin 12 weeks after injection of 300 μg (20 μg was shown by the British Medical Research Council trials to confer some protection[11]), the service program consists of a single injection at 28 weeks' gestation, with the same blood screening intervals, techniques and treatment after delivery as were followed in the clinical trial. If Rh isoimmunization occurs despite the injection at 28 weeks' gestation, the service program will be extended to consist of injections of Rh immune globulin at 28 and 34 weeks' gestation.

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# Antenatal prophylaxis of Rh isoimmunization: 28-weeks'-gestation service program

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**Two (0.18%) of 1086 Rh-negative primigravidas or multigravidas treated similarly in all previous pregnancies, who were given a single injection of Rh immune globulin (300 μg) at 28 weeks' gestation and subsequently were delivered of Rh-positive babies, had demonstrable Rh isoimmunization at the time of that injection and must be considered "logistic" failures of antenatal prophylaxis. The remaining 1084 (who were treated again after delivery) had no evidence of Rh isoimmunization at delivery and none of the 512 screened at 6 months after delivery appeared to be immunized. If the 28th-week injection had not been protective, one would have expected 14 of the 1084 to have been demonstrably Rh isoimmunized and evidence of Rh isoimmunization to have persisted in 6 of the 512 observed 6 months after delivery.**

**Six of 719 Rh-negative multigravidas who had not received Rh immune globulin after previous pregnancies or had been treated only after delivery showed evidence of Rh isoimmunization despite a single injection of Rh immune globulin at 28 weeks in a subsequent pregnancy. In three of the six the cause was most likely "sensibilization" due to previous exposure to Rh-positive blood or an untreated Rh-positive pregnancy. In 3 of the remaining 716 (0.42%) there may have been true failure of antenatal Rh prophylaxis administered at the 28th week. One would have expected this figure to be 12 of 716 if antenatal Rh prophylaxis at 28 weeks' gestation were totally unsuccessful.**

**It is concluded that a single intramuscular injection of Rh immune globulin, 300 μg, is 88% effective in preventing Rh isoimmunization during pregnancy in Rh-negative primigravidas and in multigravidas treated antenatally in all previous pregnancies, and is 75% effective in preventing Rh isoimmunization in Rh-negative multigravidas untreated during previous pregnancies. The majority of failures are due to Rh isoimmunization during pregnancy prior to antenatal prophylaxis at 28 weeks.**

**Sur 1086 primigravides et multigravides Rh négatif ayant été traitées de la même façon aux grossesses précédentes, qui ont reçu une seule injection d'immunoglobuline Rh (300 μg) à la 28e semaine de la grossesse et qui subséquemment ont donné naissance à un bébé Rh positif, 2 (0.18%) ont démontré une isoimmunisation Rh au moment de cette injection et doivent être considérées comme des échecs de "logistique" en ce qui a trait à la prévention prénatale. Les 1084 autres femmes (qui ont été traitées encore après l'accouchement) n'ont montré aucun signe d'isoimmunisation Rh lors de l'accouchement et aucune des 512 testées systématiquement 6 mois après l'accouchement n'a semblé être immunisée. Si l'injection à la 28e semaine n'avait pas protégé, on se serait attendu à ce que 14 de ces 1084 patientes montrent une isoimmunisation Rh et à ce qu'il y eut persistance des signes d'isoimmunisation Rh chez 6 des 512 patientes observées 6 mois après l'accouchement.**

**Sur 719 multigravides Rh négatif qui n'ont pas reçu d'immunoglobuline Rh lors de leurs grossesses précédentes ou qui avaient été traitées seulement après la grossesse, 6 ont montré des signes d'isoimmunisation Rh en dépit de l'injection d'immunoglobuline Rh à la 28e semaine d'une grossesse subséquente. Chez trois des six patients la cause la plus probable est une sensibilisation due à une exposition antérieure à du sang Rh positif ou à une grossesse Rh positif traitée. Chez 3 des 716 autres femmes (0.42%) il peut y avoir eu échec réel du traitement préventif prénatal Rh administré à la 28e semaine. On aurait put s'attendre à un chiffre de 12 sur 716 si la prévention prénatale à la 28e semaine de la gestation était complètement sans succès.**

**On conclut qu'une seule injection intramusculaire de 300 μg d'immunoglobuline Rh est efficace à 88% dans la prévention de l'isoimmunisation Rh durant la grossesse chez les primigravides Rh négatif et chez les multigravides Rh négatif qui ont été traitées avant la naissance durant chacune de leurs grossesses précédentes; elle est efficace à 75% chez les multigravides Rh négatif qui n'ont pas été traitées durant leurs grossesses précédentes. La majorité des échecs est due à une isoimmunisation Rh durant la grossesse survenant avant de recevoir le traitement préventif prénatal à la 28e semaine.**

As a result of the evidence of the occurrence of Rh isoimmunization during pregnancy and its successful prevention by antepartum intramuscular administration of approximately 300 μg of Rh immune globulin ($Rh_o$[D] immune globulin, Connaught Laboratories, Toronto) at 28 and 34 weeks' gestation, a service program of antenatal Rh prophylaxis was begun in Manitoba July 1, 1975. Because of calculations, based on a half-life of IgG of about 28 days, that 20 to 30

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